



Research Paper

Identification of HLA-I restricted epitopes in six vaccine candidates of *Leishmania tropica* using immunoinformatics and molecular dynamics simulation approaches

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ABSTRACT

In spite of numerous studies on vaccination for various species of *Leishmania*, research on the development of an effective vaccine for *L. tropica* is very scarce. *In silico* epitope prediction is a new way to survey the best vaccine candidates. Here, we predicted the best epitopes of six *L. tropica* antigens with vaccine capability against this pathogen, using highly frequent HLA-I alleles. Based on the frequent HLA alleles, the protein sequences were screened individually using four different MHC prediction applications, namely SYFPEITHI, ProPredI, BIMAS, and IEDB. Several *in silico* assays including clustering, human similarity exclusion, epitope conservancy prediction, investigating in experimental records, immunogenicity prediction, and prediction of population coverage were performed to narrow the results and to find the best epitopes. The selected epitopes and their restricted HLA-I alleles were docked and the final epitopes with the lowest binding energy (the highest binding affinity) were chosen. Finally, the stability and the binding properties of the best epitope-HLA-I combinations were analyzed using molecular dynamics simulation studies. We found ten potential peptides with strong binding affinity to highly frequent HLA-I alleles that can be further evaluated as vaccine targets against *L. tropica*.

1. Introduction

Leishmaniasis is a group of diseases caused by several species of genus *Leishmania* (Steverding, 2017). The most common clinical forms of leishmaniasis include visceral leishmaniasis¹ (VL), cutaneous leishmaniasis² (CL), and mucocutaneous leishmaniasis³ (MCL) (Pace, 2014).

Despite a large number of leishmaniasis cases and even the high mortality rate of VL, there is no approved and available vaccine for any of their clinical forms (Gillespie et al., 2016; World Health, 2010). Given the side effects of drugs used for the treatment of leishmaniasis and the rising number of drug resistant strains (van Griensven et al., 2010), the development of effective vaccines would be an essential mean to control this set of tropical diseases.

L. tropica is a neglected *Leishmania* species which causes mainly CL and rarely VL in many parts of the world, especially in countries located in the Middle East and North Africa (Akhoundi et al., 2016; Rostamian

and Niknam, 2018; World Health, 2010). However, compared to other CL- or VL-causing *Leishmania* species, studies on *L. tropica* are scarce (Rostamian and Niknam, 2018), particularly with respect to its vaccine development which has no report in the literature except our previous work (Rostamian et al., 2018). Furthermore, *L. tropica* is biochemically, serologically, and genetically heterogeneous (Rostamian and Niknam, 2018). The pathology of *L. tropica* is also different from other common *Leishmania* species, such as *L. major*, in both humans and experimental models (Bastien and Killick-Kendrick, 1992; Rostamian and Niknam, 2018). Given these issues, further studies on *L. tropica* are required.

Despite the role of CD8+ T cells in tissue damage, several studies have clearly shown that their activation is required to control *Leishmania* infections. The CD8+ T cells can not only take part in primary responses but they also can actively participate in resistance to the reinfection (Basu et al., 2007; Belkaid et al., 2002; da Conceicao-Silva et al., 1994; McElrath et al., 1988; Muller et al., 1994). Thus, it

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¹ VL: visceral leishmaniasis.

² CL: cutaneous leishmaniasis.

³ MCL: mucocutaneous leishmaniasis.

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